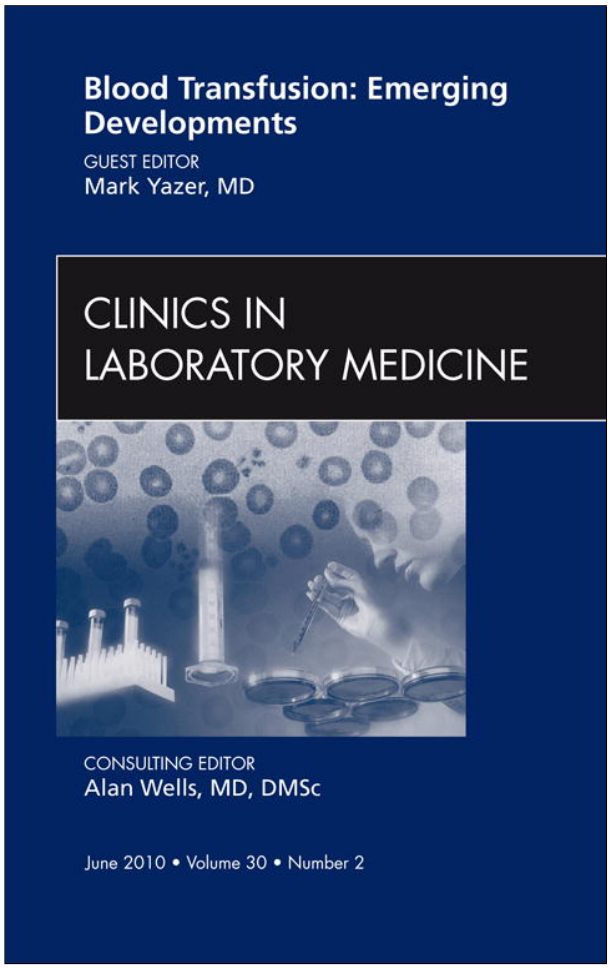

Governance in the European Union: The European Blood Directive as an Evolving Practice

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KEYWORDS

• European Blood Directive • Blood donation
• Blood policy • Donor eligibility

This article reconstructs governance practices related to blood policy that have developed within in the European Union (EU) over the last 15 years. It describes core aspects of the policy and argues that, despite an integrated cooperative approach between policy-makers and practitioners, this policy remains an open and evolving process. The European Blood Directive (2002/98/EC) and its subsequent directives managed, for the first time, to create an overarching framework for transfusion procedures. This framework consists of a number of standard definitions as well as detailed standard operating procedures (SOPs), yet leaves room for interpretation and different practices between EU member states. A recently published report on the progress of transposition of the Directives into national legislation reveals different standards, suggesting a lack of uniformity of safety and quality requirements. Further, gaps in the directives amount to practical medical problems, while increased mobility among EU citizens may add further problems to achieving the objective of a self-sufficient supply of blood and blood products. This might undermine public confidence in the quality of blood products and the health protection of donors, which, in turn, must be countered by a cooperative effort of policy-makers and blood establishments.

Blood policies have been on the agenda of the European Community for more than 15 years. They pertain to both qualitative as well as quantitative issues; that is, assuring the quality and safety of blood and its derived products while simultaneously ensuring its availability in sufficient quantities. As early as 1994, the European Commission identified the need for a comprehensive strategy.[1,2] Voluntary, unpaid donations were meant to ensure self-sufficiency in blood and plasma, for which the

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Clin Lab Med 30 (2010) 489–497
doi:10.1016/j.cll.2010.02.008 **labmed.theclinics.com**
0272-2712/10/$ – see front matter

Commission needed to learn about European citizens' perception and understanding of blood-related issues as well as citizens' attitude toward donating.

A survey among citizens of the EU revealed that "citizens are reasonably well-informed about general blood issues but several misconceptions do exist reflecting the need for further information and education programs about blood and plasma donation."[3] To this end, the report was meant to "be of value to national health authorities, blood collection and transfusion organizations, blood donor associations, and the plasma products industry in their efforts to contribute to achieving the goal of Community self-sufficiency in blood and plasma."[3]

The remainder of this article specifies how these objectives were meant to be achieved—yet how they remain an unfinished process. To this end, the article details the content of the European Blood Directive and some of its subsequent specifications that were meant to build an overarching framework across EU member states. It then sets out to analyze a recently published report on the transposition progress of the directives into national legislation. The report reveals that differences continue to exist between member states on a number of factors. Further problems on the road toward a safe and self-sufficient supply stem from gaps in the directives, causing medical problems, as well as from (potential) social and political developments. From these considerations, it can be concluded that despite the creation of blood directives at the EU level, the governance of blood remains an ongoing process and a site of construction.

BLOOD POLICY IN THE EU: DEVELOPING DIRECTIVE 2002/98/EC

In the aftermath of the 1995 survey, a concerted effort to ensure sufficient supplies was brought under way. It developed in cooperation between the European Commission as the authoritative norm-setter as well as the European Blood Alliance (EBA) that was founded in autumn 1998. The EBA consists of members "with a spectrum of organization arrangements ranging from the centrally managed national services (…) to local and regional services."[4] Their aim is to increase awareness in the public and among professionals as to the non-remunerated donation of blood and the preparation of its components for therapeutic purposes; to provide technical and professional support to members; and to develop facilities for and coordinate information-sharing on a national, European, and global level. In 2006, blood donations from EBA members' blood services amounted to around 15.5 million donations from a population of just over 300 million people.[4] For comparison, there were approximately 9.6 million allogeneic blood donors in the United States in the same year.[5] In the meantime, the EBA commented on and contributed expert advice to the European Blood Directive (EC/2002/98).

Directive 2002/98/EC and its Successors

The Blood Directive from 2002 was the first and groundbreaking attempt to devise uniform standards of quality and safety for human blood and its components. It did so by defining minimum safety criteria with a view to contributing to public confidence in terms of the quality of blood and blood products, as well as health protection of the donors. In line with the initial objectives of 1994, further intentions were to attain self-sufficiency and enhance confidence in the safety of the transfusion chain. The directive is binding for member states of the EU but it leaves open the choice of form and methods to comply, which includes the possibility of introducing more rigorous standards. Directive 2002/98/EC is termed the Mother Directive because it functions as a standard-setter while triggering further, more specific directives.

Following 2002/98/EC were three further directives that set out technical implementation measures for issues identified in the Mother Directive. Directive 2004/33/EC pertained to technical requirements for blood and blood components. Directive 2005/61/EC specified traceability requirements and requirements for the notification of serious adverse reactions and events. Finally, Directive 2005/62/EC provided standards and specifications relating to a quality system for blood establishments, similar to those established by the American Association of Blood Banks in the United States.[2] As Listl and Klouche[1] note, these directives were vital for the harmonization of European blood and blood-component comparability as well as transfer within Europe because they provided a catalog of definitions that did not exist previously. Either central terms were not clearly defined, or regulations did not exist in some member states.

An example of the specificity is provided by Seidl and colleagues[2] with regard to the quality system entailed in the Mother Directive and Directive 2005/62/EC. Regarding the former, they list the description of the quality system to include:

1. An organization chart, including responsibilities of responsible persons and reporting relationships
2. A site master file or quality manual describing the quality system in accordance with Article 11(1)
3. Number and qualifications of personnel
4. Hygienic provisions
5. Premises and equipment
6. List of SOPs for:
   - Donor recruitment
   - Retention and assessment of donors
   - Processing and testing
   - Distribution and recall of blood and blood components
   - Reporting and recording of serious adverse reactions and events.

Specifications

On this basis, Directive 2005/62/EC sets out standards and specifications for blood establishments to ensure the safety of blood across Europe. Guidelines for a quality system were developed by a multinational project under the leadership of the German Red Cross Donor Service of Baden-Württemberg. The project entailed a consortium of sixteen members and established a project platform on the implementation of good practice. It developed a common format and regulations for SOPs to carry out an activity to demonstrate compliance with procedures,[2,6] supported by the EBA.

In the absence of absolute criteria, the quality management system developed is hierarchically structured in seven steps. They range from the framework of regulations via guidelines on document change control and personnel training to SOPs that are simple and user-friendly, listing precise quality requirements, requisites, and quality terms linked to the EU directives. At the same time, these standards cross-reference with or exist in addition to processes based on good manufacturing practice, good laboratory practice, and International Organization for Standardization (ISO) norms because blood establishments vary in size and often comprise several production sites. Such nexus of procedural regulations enables the compatibility of sites and eases exchange of supplies to external sites. The authors conclude that there is a list of benefits that includes:

- the definition of an overall quality policy
- improved personnel responsibility, qualification and training

- error and risk assessment system
- continuous improvement
- improved resource management
- performance improvement.[2]

Although the implementation process of quality control is complex, a positive cost effect is expected in the mid- to long-run, particularly if synergetic effects between the EU directives and good manufacturing practice and ISO standards can be exploited.[2,6]

THE IMPLEMENTATION PROCESS

In the run-up to a meeting of the competent blood authorities, attendees were asked to answer a ''questionnaire on the transposition and implementation of the European regulatory framework of blood and blood components.''[7] It was prepared before a meeting of competent blood authorities on January 29, 2009, comprising of EU member states, candidate countries (Croatia, Former Yugoslav Republic of Macedonia, and Turkey), and European Free Trade Association countries (Iceland, Liechtenstein, Norway, and Switzerland). The questionnaire was intended to determine whether countries had indeed transposed the four Directives into national law, reasons for a delay, and details regarding selected further issues. The report provides detailed information on:

- the national blood authority (name and address of national authority)
- transposition (has the transposition process been completed?)
- authorization (how many blood establishments are there in the country?)
- hospital blood banks (how many are there in the country?)
- inspections (is a system in place, how many inspections have been performed?)
- donor eligibility criteria (regarding exemption in accordance with Annex III.2.2.2 of Directive 2004/33/EC) (Annex III.2.2.2 of Directive 2004/33/EC: ''Persons whose sexual behavior puts them at high risk of acquiring severe infectious diseases that can be transmitted by blood.'')
- vigilance (serious adverse events and reactions)
- testing requirements
- imports and exports of blood and blood components
- sanctions (have authorizations been revoked or suspended, or have penalties been imposed?)
- others (eg, difficulties encountered in the transposition process).

The report may conclude the transposition process of the Directives but, based on the analysis of answers provided, it still leaves possibility for improving the safety of blood and blood derivates across Europe. On one hand, not all countries participating in the meeting in January 2009 provided full information on the sections above. At the time of publication on January 15, 2010 some empty spaces still had not been filled. This includes candidate and European Free Trade Association countries that are not obliged to comply with the Directives to an extent that member states must; but also some of the EU member states. On the other hand, the report also reveals that different criteria may exist across countries. This therefore leaves open the question whether blood is indeed of a uniform standard across the EU and its surrounding countries.

For instance, concerning donor eligibility criteria in EU member states for which a certain specification had to be provided, there are about four different answers.

Countries that provide a comprehensive account of exclusion criteria regarding risk-laden sexual behavior usually specify these as homosexual relations, heterosexual relations with changing partners, or unprotected intercourse, as well as intercourse for drugs or money, often in connection with prostitution. In addition, sometimes this risk group is expanded by excluding potential donors that have visited regions with a high rate of HIV or hepatitis. Countries that have expanded the sexual-practice deferral include Austria, Cyprus, Czech Republic, Denmark, France, Germany, Lithuania, the Netherlands, Slovenia, Sweden, and the United Kingdom. Romania forms a category by itself, listing the treatment for hemophilia before 1988 as the criterion for exclusion. A third group is formed by countries that answer affirmatively to whether exclusion criteria are in place (Finland, Greece, Hungary, Italy, Latvia, Luxembourg, Malta, Poland, and Portugal). Finally, Bulgaria, the Republic of Ireland, and Slovakia state that no national guidelines exist for the assessment of at risk sexual behaviors.

Table 1 provides a comprehensive overview of EU member states' testing requirements (excluding Estonia). The table reveals that there exists a consensual procedure for testing requirements for three infectious agents (hepatitis B surface antigen, anti-hepatitis C virus, and anti-HIV 1/2). However, apart from these three tests, member states proceed unilaterally. Some even demand further tests to be conducted, as specified in the table. Nonetheless, member states exchange blood if they have the necessary procedures in place, which usually refers to the existence of compatible safety standards in the country of origin, but may include regular on-site inspections such as Germany demands. The exception is the United Kingdom, which does not export blood or blood components because of variant Creutzfeldt-Jakob disease risks. The report does not specify whether the reason is that the United Kingdom refrains from exporting voluntarily or whether this is a consequence of EU member states refusing to import blood from the United Kingdom. The latter case might be the reason, judging from Germany's policy to deny donations from people who have spent more than 10 months in the United Kingdom between 1980 and 1996.

Apart from the special role of the United Kingdom, the EU forms a relatively closed market for blood and blood components. Trade of components within the EU takes place as long as bilateral agreements and comparable minimum standards exist. However, trade in blood and blood products is not necessarily well documented, meaning that there is usually a lack of data in terms of volumes exported (and, by implication, imported). Greece claims to have imported 26,000 units of blood cells from Switzerland, a non-EU member country, during 2008, while Sweden imports plasma used as a source material for medicinal products from the United States. On the other hand, Poland exported 107,032.5 L of plasma for fractionation to other EU countries while Germany exported 1,136,060 L of plasma for fractionation without specifying the destination. France exported 55 red blood cell concentrates and 6 fresh frozen plasmas to 13 countries (Algeria, Belgium, Canada, Congo, Egypt, Gabon, Germany, Hungary, Ireland, Mali, Nigeria, Senegal, and Switzerland).[7]

Possible Problems

The primary objective of the European Community was to establish a safe and reliable supply of blood and blood products to citizens across Europe. A European Blood Directive was developed and specified in cooperation with national and regional blood establishments in the subsequent years. This effort resulted in the Mother Directive of 2002 and three directives that specified its content. Again, in practice, the specific implementation arrangements were developed by practitioners, resulting inter alia in

Table 1
Testing requirements in EU member states

	Anti HBc	HBs ag	NAT HBV	Anti HCV	NAT HCV	Anti HIV-1/2	Ag HIV	NAT HIV 1	Treponema Pallidum	HTLV	Further Tests?
Austria		✓		✓	✓	✓		✓	✓		Nonspecific immunactivating marker (eg, neopterin)
Belgium		✓		✓	✓	✓		✓	✓		Anti-HBc for new donors and on indication
Bulgaria		✓		✓		✓	✓		✓		
Cyprus		✓		✓		✓	✓		✓		CMV for immunosuppressed patients
Czech Republic		✓		✓		✓	✓		✓		
Denmark		✓	✓	✓	✓	✓		✓		✓[a]	
Finland		✓	✓	✓	✓	✓	✓	✓			According to the epidemiologic situation, extra testing may be required
France	✓	✓	✓	✓	✓	✓		✓	✓	✓	NAT HBV* In some French areas with particular epidemiologic situations (French overseas departments) Detection of malaria infectious markers. If necessary (individuals who have lived a malarial area or with history of undiagnosed febrile illness, visitors to endemic area)
Germany	✓	✓		✓	✓	✓		✓	✓		
Greece		✓	✓	✓	✓	✓	✓	✓		✓	
Hungary	✓	✓		✓		✓			✓		
Rep. of Ireland		✓		✓	✓	✓		✓			

Italy		✓	✓	✓	✓	✓		✓	✓		
Latvia		✓	✓	✓	✓	✓		✓	✓		
Lithuania	✓	✓	✓	✓	✓	✓		✓	✓		
Luxembourg	✓	✓	✓	✓	✓	✓	✓	✓	?	✓	VDRL
Malta	✓	✓		✓		✓			✓		Tests are required for: hemoglobin, liver function, anti-CMV/parvovirus (on request)
Netherlands		✓	✓	✓	✓	✓		✓	✓	✓	Parvo B19 for selected donations and bacterial culture for all platelets
Poland		✓	✓	✓	✓	✓		✓	✓		ALT
Portugal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
Romania		✓		✓		✓			✓	✓	HIV testing is performed using AG/antibody anti HIV combined kits
Slovakia	✓	✓		✓		✓	✓		✓		
Slovenia	?	✓	✓	✓	✓	✓	✓	✓	✓	?	NAT, anti HIV1/2/0 and p24Ag, HIV RNA, HCV RNA, HBV DNA are obligatory
Spain		✓	✓	✓	✓	✓		✓	✓		*Trypanosoma cruzi*
Sweden	✓	✓		✓		✓			✓	✓	Hemoglobin
United Kingdom		✓		✓	✓	✓			✓	✓	Not for mandatory donor screening. Certain additional tests may be performed, depending on need, eg, anti-CMV

Abbreviations: Ag, antigen; ALT, alanine aminotransferase; Anti, antibody; CMV, cytomegalovirus; HBc, hepatitis B core antigen; HBs, hepatitis B surface; HCV, hepatitis C virus; HTLV, human T-lymphotrophic virus; NAT, nucleic acid amplification technology.

[a] Only first time donors.

From European Commission. Summary table of responses from competent authorities for blood and blood components. Questionnaire on the transposition and implementation of the European regulatory framework blood and blood components. Brussels, Health and Consumers Directorate-General; January 15, 2010.

SOP handbooks. Meanwhile, EU member states have gradually transposed the Directive into national legislation where it is now one of standards to ensure the quality of blood and its derivative products.

However, potential problems remain, pertaining to medical as well as political issues. On the medical side, an assessment of the implementation questionnaire reveals that different standards for testing requirements exist. Given that only three common transmissible disease-testing requirements can be found across member states, one wonders whether a uniform level of quality has been achieved. Another indicator toward this conclusion can be found in the very different amount of detail provided regarding data on import and export of blood and blood products between member states or across EU borders. In a similar vein, Listl and Klouche[1] state that Directive 2004/33/EC is not specific enough in terms of the required bacteriologic control, leaving the interpretation of the implication to member states.

The other, potentially more pressing, issue is political in nature. It concerns several points. First, there is the problem of growth. During the period of developing the different blood directives, the EU grew from 15 member states in 1995 to the current number of 27. During any growth process, accession candidates are required to accept the entire *acquis communautaire*, that is, the existing legal framework of the EU. This might be a source of concern as new members may not yet have transposed directives into national legislation and standards of safety might not be in operation. Consequently, the tradability and availability of blood and blood products might be hampered. Second, a concern arises from admission criteria that are closely linked to citizens' mobility throughout and out of the EU. As Listl and Klouche[1] write, criteria in Directive 2004/33/EC ''lack explicit exclusion criteria for several relevant parasitic infectious diseases, eg, mucocutaneous leishmaniosis or trypanosomiasis, while other guidelines regarding for instance toxoplasmosis, do only apply to blood but not to plasma destined for fractionation. In view of the occurrence of some of these infectious diseases in certain European countries, the continuous presence of immigrants from endemic countries, and the extent of international travel, these risks may not have received sufficient attention.''[8] Third, exclusion criteria might run counter to EU regulations that not only seek to promote mobility but also adhere to the principle of nondiscrimination. Although some countries have explicitly excluded certain risk groups from donation, as noted previously, a few member states have not. This might, one day, result in a ruling by the European Court of Justice. Fourth, related to the previous point, eventually certain criteria might reduce the pool of potential donors. Unforeseen risks may diminish the potential for interchangeability of blood and blood products, similar to the case of the United Kingdom that does not export because of the risk of variant Creutzfeldt-Jakob disease.

SUMMARY

These considerations amount to the insight that, despite the formulation of the European Blood Directive in 2002 and its subsequent implementation and specification, blood policies in the EU remain a work in progress. Social and political developments will require adjustments and specifications in the future. At the same time, policies need to be devised to maintain a pool of (reliable) donors. As much as barriers (read: exclusion criteria) might counteract this objective, a continuous effort into positively swinging public opinion toward donation seems needed. This is likely to involve both the European Commission and practitioner organizations such as the EBA in the near future.

ACKNOWLEDGMENTS

Research assistance from Torben Schenk and Ilyas Saliba is gratefully acknowledged.

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